REMARKS

A. Status of the Claims

Claims 1-73 were pending prior to the Office Action dated June 22, 2004. Claims 3, 4, 6, 7, 13, 14, 16, 17, 27, 28, 30, 31, and 34-35 have been withdrawn. Claims 1, 2, 5, 11, 12, 15, 20, 25, 26, 29, 32, 33, and 36 have been amended. Claims 74-81 have been added. Support for the amendments may be found throughout the specification, for example, at page 57, lines 4-8 and 17-26, and in the originally filed claims. No new matter has been added.

B. Amendment to Specification

The Sequence Listing has been resubmitted to correct the clerical error in which the sequences for SEQ ID NO:1 and SEQ ID NO:2 were inadvertently switched. The specification makes it clear to the skilled artisan that the sequences in the listing were switched because SEQ ID NO:1 is referred throughout the specification as a nucleic acid sequence and SEQ ID NO:2 is consistently referred to as an amino acid sequence. As such, the amended Sequence Listing properly reflects this identifying as SEQ ID NO:1 the sequence that was identified in the initial Sequence Listing as SEQ ID NO:2. Similarly, the amended Sequence Listing identifies as SEQ ID NO:2 the sequence that was identified in the initial Sequence Listing as SEQ ID NO:1.

Moreover, minor amendment to the specification has been made to clarify what one of ordinary skill understands regarding the terminology used for molecular biology. The amendment does not add new matter to the application.

On page 5, line 3, the phrase "encoded by" has been replaced with "included in."

On page 5, line 17, the phrase "encoded in" has been amended to "encodes". This change is reflected in claim 12.

On page 5, line 18, the phrase "encoded by" has been replaced with "comprises," which is reflected in claim 15.

On page 28, line 15, the term "encode" is replaced with "comprise."

C. Claims 1-2, 5, 8-12, 15, 18-26, 29, 32, 33, 36, and 39 Are Definite

The Action rejects claims 1-2, 5, 8-12, 15, 18-26, 29, 32, 33, 36, and 39 under 35 U.S.C. § 112, second paragraph, as indefinite because the sequences for SEQ ID NOs:1 and 2 were switched. The corrected sequence listing addresses this issue.

D. Claims 1, 8-11, 20-25, 32, and 39 Are Adequately Described

The Action rejects claims 1, 8-11, 20-25, 32, and 39 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement because the specification allegedly does not contain a written description in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention. It contends the specification discloses a single isolated cDNA sequence and that this does not adequately describe the of subgenera, including full length genes. The Action argues that the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides. It concludes that because the genus is highly variant, the disclosure of a specific nucleotide sequence and the ability to screen is insufficient to describe the genus. Applicants respectfully traverse this rejection.

The rejected claims are directed to an "isolated and purified polynucleotide comprising a nucleic acid sequence encoding at least [20, 50, 150] contiguous amino acid residues of SEQ ID NO:2" (claims 1, 8-9) or "comprising at least 1.5 contiguous kilobases of SEQ ID NO:1" (claim 10). The Action also rejects claims directed to an expression vector "comprising a nucleic acid sequence encoding at least 20 contiguous amino acid residues of SEQ ID NO:2" (claim 11) and such expression vectors reciting promoters (claims 20-22) or viral vectors (claims 23-24), as well as a "recombinant host cell comprising a nucleic acid sequence encoding at least 20 contiguous

amino acid residues of SEQ ID NO:2" (claim 25). The Action also rejects claims directed to a " method of preparing recombinant WWOX comprising: (a) transfecting a cell with a polynucleotide comprising a nucleic acid sequence encoding at least 20 contiguous amino acid residues of SEQ ID NO:2; and (b) maintaining the transformed host cell under biological conditions sufficient for expression of the polypeptide in the host cell" (claim 32) and where the nucleic acid sequence used in the method is a vector (claim 39).

The Federal Circuit has stated that the test for the written description requirement is "whether the application relied upon 'reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter.'" *In re Daniels*, 144 F.3d 1452, 1456, 46 USPQ2d 1788, 1790 (Fed. Cir. 1998). See also *Markman v. Westview Instruments, Inc.* 52 F.3d 967, 34 USPQ 2d 1321 (Fed. Cir. 1995) (en banc) ("Claims must be read in view of the specification, of which they are a part."). In rejecting a claim under the written description requirement of 35 U.S.C. §112, first paragraph, the Examiner has the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined in the claims. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). Accordingly, the Examiner is required: (1) to set forth the claim limitation not described; and (2) to provide reasons why a person skilled in the art would not have recognized the description of the limitation in view of the disclosure of the application as filed. *Interim Guidelines for the Examination of Patent Applications Under 35 USC 112, Paragraph 1*, Chisum on Patents, vol. 3, §7.04[1][c].

The Guidelines state that the "written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying

characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus."

In this case, the claims recite specific structures for the polynucleotides. The claims make it clear that that polynucleotides, expression vectors, and recombinant host cells include a nucleic acid sequence encoding at least 20 contiguous amino acid residues of SEQ ID NO:2. The specification fully discloses SEQ ID NO:2. The specification fully supports any polypeptide that meets the limitations of the claims. In fact, from a pure mathematical point of view, the number of species disclosed by the specification with respect to each claim is numerous. For example, with respect to rejected claim 1, a person of ordinary skill in the art would understand that the specification disclosed at least thousands of different species with respect to SEQ ID NO:2. Even an undergraduate student who has taken an elementary molecular biology course could identify many different species that satisfied the claim based simply on the disclosed sequence.

Thus, the specification satisfies the written description requirement because it reasonably conveys to one of skill in the art that they had possession of the claimed subject matter. *In re Daniels*, 144 F.3d 1452, 1456, 46 U.S.P.Q.2d 1788, 1790.

In the Examples disclosed in the Interim Guidelines, the explanation provided for Example 13 and protein variants indicates the rejected claims meet the requirements for written description. The first claim provided in Example 13 recites SEQ ID NO:3, which is said to satisfy the requirement because "each member of the genus shares SEQ ID NO:3 as a necessary common feature," contrary to the second claim in that example in which variants of SEQ ID NO:3 are claimed. With respect to the present case, each member of the claimed genus shares a

nucleic acid sequence encoding the recited portion of SEQ ID NO:2 as a "necessary common feature." Moreover, unlike the second claim in that example, there are common structural attributes that identify members of the genus, again, namely the contiguous amino acid regions of SEQ ID NO:2.

A patentee does not need to describe every embodiment on which the claim reads. According to the Federal Circuit, "[i]t is well-established that a patent applicant is entitled to claim his invention generically, when he describes it sufficiently to meet the requirements of section 112." *Amgen v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2D 1016, 1027 (Fed. Cir. 1991); *see also Utter v. Hiraga*, 856 F.2d 993, 998, 6 USPQ2D 1709, 1714 (Fed. Cir. 1988) ("A specification may, within the meaning of 35 U.S.C. §112, paragraph 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses.").

The written description requirement has been extensively addressed by the Federal Circuit. In particular, the Federal Circuit has stated that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.'" *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ 2d 1227, 1232 (Fed. Cir. 2000). The Federal Circuit has also noted that "[if] a person or ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met." *In re Alton*, 76 F.3d 1168, 1175, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996).

The Action's reliance on *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997) is misplaced because this case is readily distinguishable. A copy is provided for the Examiner's convenience as Exhibit B. In *Regents of UC*, the patentee claimed a human insulin cDNA but had disclosed the sequence of only a rat insulin cDNA. It was evidence in that case that the patentee did not have a single sequence that qualified as a human insulin cDNA. In stark contrast, the claims in this case are directed to nucleic acid sequences encoding at least [20, 50, 150] contiguous amino acid residues of **SEQ ID NO:2** or having at least 1.5 contiguous kilobases of **SEQ ID NO:1**. The full-length cDNA and polypeptide sequences for human WWOX are provided in this application and the present claims recite limitations directed to these sequences. The Federal Circuit in *Regents of UC* stated:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus.

Regents of UC, 119 F.3d at 1568. The rejected claims recite the generic formula; consequently, the genus is adequately described.

The Action contends that "Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure." Action at page 4. This is incorrect. As discussed above, any of the compounds within the genus concern nucleic acid sequences encoding at least 20 contiguous amino acid residues of SEQ ID NO:2. Contrary to the situation in *Regents of UC* and the Action's assertions, the present claims do not recite a nucleic acid sequence that is limited only by function.

In accordance with the Federal Circuit's requirements pertaining to written description, one of ordinary skill in the art would have understood that Applicants were in possession of a polynucleotide, expression vector, or host cell that included a nucleic acid sequence encoding at least [20, 50, 150] contiguous amino acid residues of SEQ ID NO:2 or having at least 1.5 contiguous kilobases of SEQ ID NO:1.

Moreover, the specification provides relevant information regarding the WWOX polypeptide structure and its activity. In Example 1 under the subheading "WWOX protein structure," two putative WW domains were identified as amino acids 18-47 and 59-88. A set of experiments employed the WW domains of WWOX in binding studies, as shown on page 131. Moreover, there is a discussion regarding WW domains on pages 22-24.

Additionally, FIG. 2 illustrates aspects of the WWOX structure, and in the relevant figure legend (on pages 15-16), the specification indicates that the "WW domains are boxed and conserved tryptophans and prolines are shown in bold. . . ." It also states, "The short dehydrogenase domain is underlines and the conserved residues YXXXK and S. characteristic of a substrate binding site, are highlighted; bases GXXXGXG, typical of a coenzyme binding site, are shown in bold italics."

Based on the foregoing, it is respectfully requested that the written description rejection be withdrawn.

E. Claims 1, 2, 5, 8-12, 15, 18-20, 25, 26, and 29 Are Not Anticipated

1. Bednarek *et al.* Is Not Proper Prior Art

The Action rejects claims 1, 2, 5, and 8-10 under 35 U.S.C. § 102(a) as being anticipated by Bednarek *et al.*, *Cancer Research*, 60:2140 (2000) ("Bednarek reference").

The Declaration of C. Marcelo Aldaz under 37 C.F.R. § 1.132 in view of *In re Katz* ("Katz Declaration") (Appendix A) shows that the Bednarek reference is the inventors' own

work. It also states why other authors of the Bednarek reference did not qualify as inventors on the present application. The Katz Declaration is evidence that the Bednarek reference is not proper prior art, and thus, it cannot anticipate the claimed invention.

Accordingly, Applicants respectfully request the rejection be withdrawn.

2. WO 01/44466 Is Not Proper Prior Art

The Action rejects claims 1-2, 5, 8-12, 15, 18-20, 25, 26, and 29 under 35 U.S.C. § 102(e) as being anticipated by WO 01/44466.

However, this reference is a PCT publication and is not a U.S. patent. The PCT application indicates it was filed on December 15, 2000 and the priority applications does not appear to have been filed in the U.S. Consequently, based on the presented evidence, it appears that the effective 102(e) date of this application is not before the priority date of the present application. Therefore, WO 01/44466 does not qualify as prior art under 35 U.S.C. § 102(e).

Furthermore, Applicants note that new claims 74-81, which recites a polynucleotide comprising a nucleic acid sequence encoding SEQ ID NO:2 or comprising SEQ ID NO:1 are not anticipated because residue 282 is a proline in SEQ ID NO:2 and this is an alanine in SEQ ID NO:33 of the cited reference. Moreover, the priority document does not contain any disclosure of host cells, which is recited in claims 26 and 29. Accordingly, this reference does not teach elements of claims 26 and 29, as well as claims 74-81.

Applicants respectfully request this rejection be withdrawn.

F. Claims Are Not Rendered Obvious

1. WO 01/44466 Cannot Be Used As Prior Art

The Action rejects claims 1, 2, 5, 8-12, 15, 18-26, and 29 under 35 U.S.C. §103(a) as being unpatentable over WO 01/44466 and Applicants' statements regarding vectors and promoters on pages 37-40 of the specification. Applicants respectfully traverse this rejection.

As discussed above, there is no evidence that this reference qualifies as prior art. Accordingly, it cannot be used as the basis for an obviousness rejection.

Furthermore, that Applicants' specification identifies a number of types of promoters and names specific promoters does not mean that claims 21-22 are rendered obvious. Similarly, the discussion of viral vectors does not render obvious claims 23-24.

"The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." MPEP § 2143.01 citing *In re Mills,* 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

Nowhere in the cited reference is there any mention of heterologous promoters, constitutive promoters, tissue-specific promoters, inducible promoters, or a noninducible promoters, which are recited in the rejected claims. It appears the cited reference states only "promoter," and provides no other qualifications. The Action does not identify any other reference that suggests these elements of the claims. A similar situation exists regarding the vector claims reciting viral vectors (claims 23-24). The Action does not provide any reason why viral vectors or specific viral vectors are obvious, except to refer to Applicants' specification at pages 37-40. Not only do these pages not discuss viral vectors, but there is no admission in them that the cited prior art document discloses or suggests such vectors. Consequently, claims 21-24 are not obvious over the cited reference because 1) the prior art reference does not teach or suggest all the claim limitations and 2) there is no suggestion or motivation to modify the cited reference. Both are required to make a proper *prima facie* case. MPEP § 2142.

As discussed above, the priority document does not mention host cells. Consequently, elements of rejected claims 25-26 and 29 are not taught and cannot be rendered obvious.

Therefore, Applicants respectfully request this rejection be withdrawn.

2. WO 02/12544 Is Not Proper Prior Art and Does Not Make Obvious the Claimed Invention

The Action rejects claims 1-2 and 8-9 as unpatentable under 35 U.S.C. §103(a) over WO 02/12544. It contends that this reference reads on SEQ ID NO:1 and clearly suggests the conversion of the amino acid sequence into a nucleic acid sequence to be used as a probe. The only difference between the reference and the instant claims is said to be that the claims are directed to nucleic acid sequences. Applicants respectfully traverse this rejection.

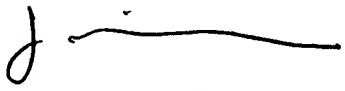
The cited reference has a priority date of August 7, 2000. The Bednarek reference, with the publication date identified on the reference as April 15, 2000, and the Katz Declaration provides sufficient evidence that this application was not filed "before the invention by applicant" as is required under 35 U.S.C. §102(e). Accordingly, it is not prior art. Consequently, it cannot be used as the basis for an obviousness rejection. Applicants respectfully request this rejection be withdrawn.

CONCLUSION

Applicants believe that the foregoing remarks fully respond to all outstanding matters for this application. Applicants respectfully request that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at 512-536-3018 is respectfully requested.

Respectfully submitted,



Gina N. Shishima
Reg. No. 45,104
Attorney for Applicant

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 474-5201
(512) 536-4598 (facsimile)

Date: 9/22/04